Estimating Conductivity Distribution of Transmural Wedges of the Ventricle Using Parallel Genetic Algorithms

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Abstract

In this work we use a computational human left ventricular wedge to simulate regions of abnormal intra- and extra-cellular conductivities that mimic some known pathological conditions. We propose a method based on genetic algorithms that aims on estimating the distribution of intra- and extra-cellular conductivities, by comparing cardiac simulations to some given transmural electrograms. The methods were developed for distributed systems and the results were obtained in a cluster composed of 8 computers interconnected by a fast network switching device. The results suggest that the proposed method is able to approximately estimate both intra- and extra-cellular conductivity distributions from transmural electrograms with an accuracy of 40%.

1. Introduction

Computational modeling of left ventricular wedges has recently demonstrated to be a useful tool for the investigation and comprehension of the complex biophysical processes that underlie cardiac electrophysiology [1, 2]. Modern Computational Wedges (CWs) take into account detailed properties of cardiac fiber and sheet transmural distributions, extra- and intra-cellular conductivities, and the dynamics of several myocyte ionic currents. CWs are able to simulate cardiac electrical activity and transmural ECGs similar to those obtained in animal experiments [3]. Studies using CWs have successfully simulated transmural ECGs that resemble several cardiac pathologies by altering specific model parameters, such as conductivity values and ionic current densities. In this work, we consider the inverse problem associated to CW modeling. We present a method based on parallel genetic algorithms and on the cardiac bidomain model that is able to estimate cardiac tissue properties from transmural ECGs.

There are strong evidences that cardiac bulk conductivity values and distribution change under many pathological conditions. Gap junction remodeling was found in patients with dilated cardiomyopathy (DCM), ischaemic cardiomyopathy (ICM) and myocarditis (inflammatory cardiomyopathy) [4]. Gap junction per myocyte volume strongly influences the effective cardiac intracellular conductivity and was observed to significantly decrease by 55% in DCM, 48% in ICM, and by 40% in myocarditis as compared with normal human myocardium. In [5], the passive conductivity property of regions under acute ischaemia was studied. It was shown that previous to gap junction remodeling the conductivity of the extra-cellular space is reduced due to capillary and myocyte swelling. Bio-impedance measurements of cardiac tissues under induced ischaemia support this thesis [6]. However, as opposed to the acute phase of ischaemia, during the chronic stage of infarct bioimpedance measurements show that extra-cellular conductivity increases as a result of necrosis and myocyte loss.

In this work we use a computational human left ventricular wedge [1] to simulate regions of abnormal intra- and extra-cellular conductivities that mimic some of the above mentioned pathological conditions. We propose a method based on genetic algorithms that aims on estimating the distribution of intra- and extra-cellular conductivities, by comparing CW simulations and some given transmural ECGs. Here, we assume that all the other wedge model parameters are fixed and known. In addition, the accuracy of the estimation is tested with simulated transmural ECGs, for which the correct conductivity values are known. The developed genetic algorithm incorporates distinct features to cope with the complexity and long execution times associated to cardiac modeling. The methods were developed for distributed systems and the results were obtained in a cluster composed of 8 computers interconnected by a fast network switching device. The results suggest that the proposed method is able to correctly estimate both intra- and extra-cellular conductivity distributions from transmural ECGs. We hope that further

developments of the described method may contribute to the better characterization and classification of cardiomyopathies.

2. The computational human left ventricular wedge

We have developed a mathematical model for the purpose of simulating electrophysiological phenomena arising from a segment or wedge of human left ventricle which is assumed to be in a perfusion medium or bath (a passive and isotropic conductor). The size of this ventricular tissue was chosen to be approx. 1.5 cm (endo- to epicardium) by 1.5 cm (apex to base). As shown in Figure 1, the endocardial , epicardial, apex and base surfaces interface with a homogeneous extracellular medium (bath), yielding an overall tissue-bath dimension of 3.0 x 3.0 cm.

Our simulations are based on bidomain equations, which can account for both the intracellular and extracellular domains of this cardiac tissue. The functional coupling of these two domains is accomplished using non-linear sets of equations which describe the transmembrane ionic currents that are generated across the sarcolemma of the human ventricular myocyte. This has been as described in detail by ten-Tusscher et al.[7] In accordance with published cellular electrophysiological data, three distinct ventricular myocyte phenotype or mathematical models were utilized in these calculations: epicardial, M and endocardial cells. The numerical solution of this large non-linear partial differential system yields spatial distributions and temporal characteristics of the extracellular potential (ϕ_e), intracellular potential (ϕ_i) and transmembrane potential (V_m). Santos et al. [8] have developed the numerical methods for efficiently solving this bidomain mathematical model.

All bidomain parameters were based on those reported in previous work.[1] 3D orthotropic conductivity tensors that vary in space were used to replicate the laminar fiber structure of the heart, where σ_e and σ_i stand for the extracellular and intracellular conductivity tensors, respectively. The cardiac tissue conductivity values from the literature have been uniformly rescaled to match the reported apex-to-base (70 cm/s) and transmural conduction velocities (45 cm/s) in the mammalian ventricles. The bath conductivity was set to 20 mS/cm. The capacitance per unit area and the surface area-to-volume ratio are set to 2 μF/cm2 and 2000 /cm, respectively. The spatial and temporal discretization steps of the numerical model are set to 150 μm and 50 μs, respectively. All simulations were carried out for a minimum of 350 ms after a single current stimulus was introduced at a selected endocardial site.

The extracellular potentials dve, i.e. the signals which would be sensed by transmural leads were calculated by taking the difference of the simulated extracellular potentials (ϕ_e) at the endocardial and epicardial boundary points. The positions of such virtual electrodes are illustrated in Figure 1.

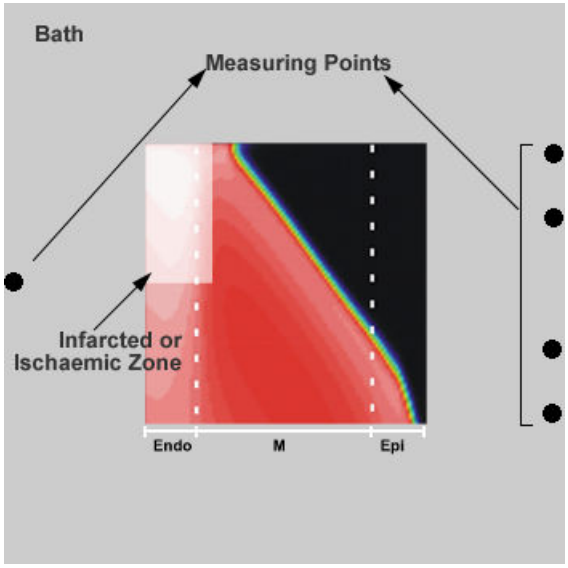

Figure 1. Computational preparation of a human left ventricular wedge immersed in a perfusing bath.

We modified the extracellular and intracellular conductivity values of a specific and small rectangular region of 0.3 x 0.7 cm near the endocardial, as illustrated in Figure 1. We consider the extracellular (intracellular) tensor, σ_e (σ_i), to be isotropically modified by a scalar α (β). Therefore the extracellular and intracellular tensors in the the specified region are $\alpha\sigma_i$ and $\beta\sigma_e$, respectively. This way the anysotropy or rather orthotropy of the tissue is kept unmodified. Two different cases were simulated with different (α, β) parameters. The first mimics the situation of acute ischaemia, and $(\alpha, \beta) = (0.1, 0.65)$ takes into account the observations reported in [5]: down-regulation of gap-junctions leads to a decrease of intracellular conductivity; and reduction of extracellular volume due to myocyte swelling leads to decrease of extracellular conductivity. The second simulation reproduces the case of a chronic infarcted region taking $(\alpha, \beta) = (0.05, 2.0)$, i.e., reproducing the reduction of intracellular space and conductivity due to myocyte loss, and corresponding increase of extracellular space and conductivity, as previously reported in [6]. Figure 2 shows the simulated transmural ECGs of a normal wedge $(\alpha, \beta) = (1.0, 1.0)$, a wedge with a ischemic region $(\alpha, \beta) = (0.1, 0.65)$, and wedge with a infarcted region $(\alpha, \beta) = (0.05, 2.0)$.

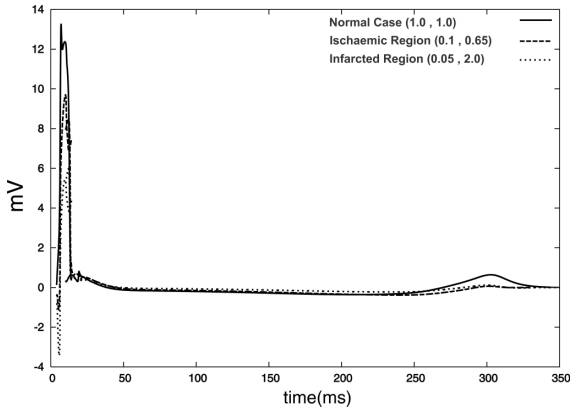

Figure 2. Simulated transmural electrograms for a normal wedge, parameter (1.0,1.0), for a wedge with a region under acute ischaemia (0.1,0.65), and for a wedge with a chronic infarcted region (0.05,2.0)

3. Genetic algorithm for the inverse problem

We propose a method based on genetic algorithms [9] that aims on estimating the intra- and extra-cellular conductivities of a known and restricted region of the computational human left ventricular wedge described above. The method tries to estimate the parameters (α, β) by comparing simulated transmural ECGs to some given or observed transmural ECGs. Here, we assume that all the other wedge model parameters are fixed and known. In addition, the accuracy of the estimation is tested with simulated transmural ECGs, for which the correct conductivity values are known, i.e. the observed transmural ECGs are also artificial. The inverse problem can be formulated as:

$$\min_{(\alpha,\beta)} F(\alpha, \beta) \quad (1)$$

$$F(\alpha,\beta) = \frac{\sum_{i=1}^{np} \sqrt{\sum_{j=1}^{nt} (vde_{(\alpha,\beta)}(i,j) - vde_o(i,j))^2}}{np\, nt} \quad (2)$$

where i is from 1 to np, np is the number of transmural derivations. In our case as illustrated in Figure 1 $np = 4$. $vde_o(i,j)$ is the ith observed transmural electrogram at point jdt, where dt is the sampling rate or time discretization, j is from 1 to nt, nt is the total number of discretizations. $vde_{(\alpha,\beta)}$ are the simulated transmural electrograms for a given (α, β).

The genetic algorithm searches for the parameters (α, β) that minimize the fitness function F given by Equation 2. Each candidate (α, β) is treated as a chromosome and is represented by a word of 14 bits. The first seven bits represent α and the last seven bits represent the parameter β parameter. Our genetic algorithm beggins with a population of 21 chromosomes randomly chosen. For each candidate (α, β), the genetic algorithm calls the cardiac simulator which generates the set of transmural electrograms $vde_{(\alpha,\beta)}$. The genetic algorithm takes the simulated results and computes the fitness of the candidate (α, β) by casting Equation 2. The generations of new candidates is based on the processes of selection, crossover and mutation, as inspired by the natural selection theory of Darwin [9]. The selection of new candidates is based on the steady-state algorithm described in [9]. After ordering the candidates by their computed witnesses, the seven worst candidates are discarded and substituted by new ones. The new candidates are generated via chromosome crossover and mutation between the best actual 7 candidates. Therefore, the crossover rate is approximately 33%. Mutation rate was chosen to be 10%.

Our genetic algorithm was target to distributed environments and its parallel implementation follows the traditional master-slave parallel decomposition. A central machine, the master, is responsible for the execution of the genetic algorithm. This machine does the jobs of selection of new candidates, crossover and mutation. Each slave machine is responsible for executing an instance of the cardiac simulator for a given cadidate (α, β), as well as for calculating the fitness function of that candidate. The Message Passing Interface (MPI) library [10] was adopted for the communication between master and slave machines.

4. Results

All simulations were executed in the Laboratory of Computational Physiology, located in the Universidade Federal de Juiz de Fora, in a small Linux cluster composed of 8 nodes, each node containing an AMD Athlon 64 3GHz processor with 2 GB of main memory.

The genetic algorithm used in this work had a initial population of 21 parameter candidates (crhomosomes) that were randomly chosen. The stop criterion adopted was to evaluate 25 generations (iterations) of the genetic algorithm. The evaluation of the fitness of a parameter candidate was done by one of the slave machines and involved the forward solution of the bidomain problem for the particular conductivity values. Each execution of the cardiac simulator took about 10 minutes in a single machine.

The simulation was executed in the 8 available machines of the cluster, one was taken as the master machine and seven as slave machines. The execution of all the 21 individuals of the initial populatioan took around 30 minutes, whereas the other 24 iterations (generations) were executed in 240 minutes (24×10 minutes). Therefore, the total execution time of the genetic algorithm took around 270 minutes.

For the transmural simulated electrograms generated with the parameters (0.1 , 0.65), which mimics conductivity changes under acute ischaemia, the genetic algorithm

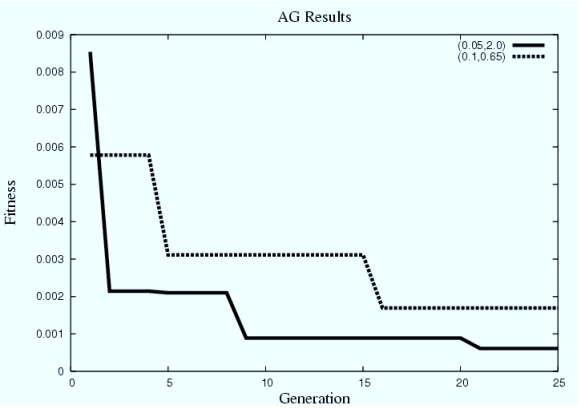

Figure 3. Evolution of the fitness of the best candidate for each computed generation of the genetic algorithm during the solution of two inverse problems: $(\alpha, \beta) = (0.1, 0.65)$ and $(\alpha, \beta) = (0.05, 2.0)$.

parameter estimatation was (0.063, 0.553). Thus, the relative error on the estimation of the extracellular (intracellular) conductivity was 15% (37%). For the transmural electrograms generated with the parameters (0.05 , 2.0), which mimics conductivity changes under chronic infarct, the genetic algorithm parameter estimatation was (0.076, 2.20). Thus, the relative error on the estimation of the extracellular (intracellular) conductivity was 20% (35%).

Figure 3 shows the evolution of the genetic algorithm by presenting the fitness of the best candidate for each computed generation. We note that after 25 iterations of the genetic algorithm the initial fitness values drops by almost an order of magnitude.

5. Conclusions

This work has presented some preliminary results related to the application of cardiac modeling on the estimation of cardiac tissue properties from information given by transmural electrograms. A parallel genetic algorithm was developed and used as the method for optimization. Motivated by the strong evidences that cardiac bulk conductivity values and distribution change under many pathological conditions, in this work we have modeled the the cardiac conductivity changes reported for acute ischaemia and chronic infarct. The parallel genetic algorithm coupled to the cardiac bidomain model was able to estimate, from given observed electrograms, cardiac tissue conductivity values with an accuracy of 40%. The execution time of the parallel genetic algorithm took around four hours in a 8-node linux cluster. Further research is necessary in order to better characterize the feasibility of the inverse procedure here described.

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